United States Environmental Protection Agency

Virtual Tissues - the Next Big Step for Computational Biology

Implications for Toxicology and Risk Assessment

Office of Research and Development
National Center for Computational Toxicology

Virtual tissues – what and why?

- Multiscale biology
  - Tissues are communities of heterogeneous cells
  - Cellular phenotype influenced by the neighborhood
  - *Given that biology determines the response to environmental stress, multiscale computational modeling of tissues is a logical step on the path towards a more complete understanding of toxicological mechanisms and correspondingly more accurate risk assessments*

Virtual tissues – what and why?

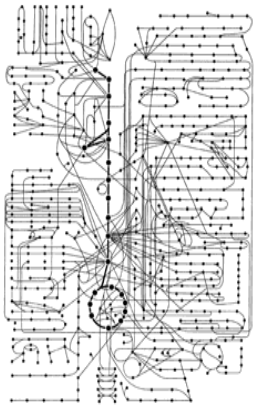
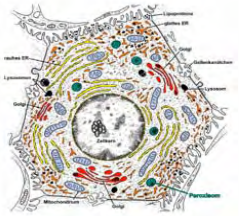
- Technology
  - First PBPK models in the late 1960's
  - Multiple orders of magnitude increases in computing power and software sophistication since then
  - Virtual tissues are technologically feasible today

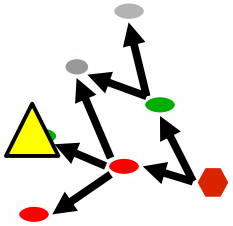
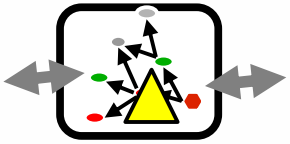
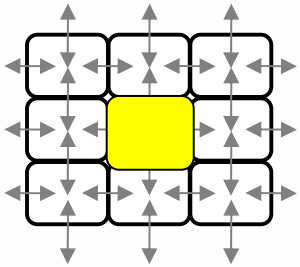
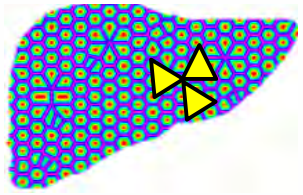
Key aspects of a virtual tissue

- More basic components inform structure and function at higher levels of organization
  - molecules → signaling networks
  - Molecules →organelles
  - Signaling networks + organelles → cells
  - Heterogeneous population of cells →tissue
- Intercellular processes
  - Signaling networks
- Intracellular processes

- Spatial organization

Multiscale computing can help quantitative modeling of liver function and injury

Molecules → Cell → Tissue → Organ

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- *A Quantitative Understanding of Dynamic Cellular Processes During Detoxification in Human Hepatocytes (Research Network Within HepatoSys)*
  - Matthias Reuss, Universität Stuttgart, Institut für Bioverfahrenstechnik
- *The National Biomedical Computation Resource: Computing Technology to Support Development of Computational Tissues*
  - Wilfred Li, San Diego Supercomputer Center, University of California, San Diego
- *Towards the Virtual Human: Development of Three Dimensional Organ Models for Human Health Risk Assessment*
  - Richard Corley, Pacific Northwest National Laboratory

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- *Mechanistic Cardiac Modeling and Risk Assessment*
  - Anna Georgieva, Novartis
- *The Virtual Liver Project at the U.S. EPA's National Center for Computational Toxicology and Its Implications for the EPS Mission to Protect Human Health*
  - Imran Shah, U.S. EPA/ORD/NCCT